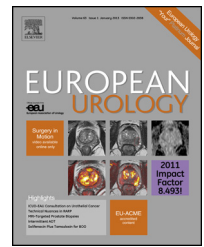


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Platinum Opinion – Collaborative Editorial

Mesh Sling in an Era of Uncertainty: Lessons Learned and the Way Forward

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For many years, synthetic mesh was avoided whenever possible for surgical treatment of stress urinary incontinence (SUI) and/or pelvic organ prolapse (POP) because of the recognized complications of fibrosis and erosion seen with Mersilene [1] and Gore-Tex slings [2].

Petros and Ulmsten [3] in 1990 and Petros and Papadimitriou [4] more recently described a fairly simple procedure with tension-free vaginal tape (TVT), during which the surgeon placed a thin strap of polypropylene mesh in a midurethral position. Since the 1990s, the marketing and use of synthetic materials for SUI and POP indications have dramatically increased. This was particularly noticeable after the publication of a randomized controlled trial comparing TVT with colposuspension [5]. A number of similar procedures were subsequently granted marketing licenses with little clinical data from adequately powered randomized studies. This was followed by a series of modifications including transobturator tape (TOT) [6] and, recently, a wave of single-incision slings, or *mini-slings*, to prevent passage of trocars through the retropubic space or obturator fossa [7]. Concomitantly, the specialty of female pelvic medicine and reconstructive surgery has witnessed the very rapid growth of larger segments of synthetic material, referred to as *mesh*, being implanted beneath the vaginal wall to correct POP based on the early data supporting efficacy of TVT and TOT.

More than 40 implants are on the market [8,9] and are used with little evidence related to mid- and long-term safety and efficacy. Training to place these new implants has often comprised cadaver courses on weekends, review of video procedures, observing “experts” performing implants, and mentorship in institutions by a visiting surgeon. The use of these materials and the surgical techniques have not been limited to subspecialist practice. In 2008, following an

escalation in complications reported to the Manufacturer and User Facility Device Experience (MAUDE) database, the US Food and Drug Administration (FDA) issued a first notification to inform the public [8] that these devices and “kits” had risks, should be used with caution, and might result in nonreversible outcomes [10]. A second FDA notification in 2011 sounded even more alarming [11] and provoked a chain reaction from patients, physicians, manufacturers, and lawyers. Similar initiatives were under way in the United Kingdom, with recognition of the problem by the Medicines and Healthcare Products Regulatory Agency (MHRA) [12,13]. As the Internet facilitated connection between desperate patients seeking help [14], television advertisements started to inform the public about issues related to “transvaginal meshes.” A number of Web sites inspired by patients’ experiences identified problems with mesh (eg, TVT Messed up Mesh [TVT Mum], <http://www.tvt-messed-up-mesh.org.uk/>).

During specialty meetings, many presentations and discussions have focused on mesh or tape complications and their management, specifically, obstruction, pain, dyspareunia, and erosion that may have irreversible consequences despite multiple interventions [10]. In daily practice, patients have begun to inquire more intensely about “mesh” or “tape,” and the regulatory authorities have provided information for patients on this subject. There is a lack of registries to establish the true incidence of the problems with the use of synthetic materials, as has been recognized with the underreporting of these complicated cases to the “optional” MAUDE database [15] and to the other regulatory bodies such as MHRA in the United Kingdom. Although voluntary registries have been established by professional groups, they do not provide accurate information because registration of all cases would be

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required and, invariably, existing voluntary registries are prone to selective reporting of cases.

Existing materials have been introduced on the basis of biocompatibility in the body. Although some initial materials were found to be associated with more problems than others, such as ObTape [16], four groups of biomaterials can be described according to pore size. With recognition of the importance of a pore size of $>75\ \mu\text{m}$ between synthetic fibers, it has been suggested that infective problems are reduced [17]. The mechanical properties of meshes have been tested industrially for resistance, pliability, elasticity, and ductile qualities. These properties depend on the type of tissue structure (woven or knitted) and the type of fiber used (mono- and multifilament). With the intention of providing a “silent” material, which does not trigger an unfavorable host-tissue reaction, introducing the foreign body induces a “scarring” response. This fibroblastic reaction replaces the inflammatory reaction, leading to progressive colonization of the prosthesis. It has been suggested that the weave of mesh is important and that open-weave prolene mesh shows unique biomechanical properties, compared with other tested materials, that might lead to reduced erosion rates [18]. Despite these observations, it was reported from the original study by Ward and Hilton that TVT mesh has a significant erosion rate of at least 4% [19]. A number of articles have raised the concern that synthetic materials might not be inert when implanted in the body [20,21].

Finally, as the first awards from individual lawsuits against reputed manufacturers became known, some companies (eg, Ethicon, Bard) decided to no longer market their mesh products. At present, several mesh-focused class-action lawsuits have made the headlines. The first federal litigation was directed at Mentor’s ObTape sling and has been settled [16], and the TVT Secur is no longer marketed. Five pelvic-repair-system products from different manufacturers are the subjects of medical device litigation in West Virginia, overseen by Judge Goodwin [22]. Several thousands of petitions are involved in each manufacturer class-action suit. In real-life practice, attorneys often send their clients to centers of expertise for mesh or tape removal and ask for retrieval of the removed parts as evidence for the case. The litigation is against the companies that produce the kits, because the material is defective or the training is improper, as well as the doctors that implant the devices. In this atmosphere, more physicians in the United States are opting for nonmesh treatments (pers. comm., S. Raz, Los Angeles, CA, USA).

Clearly, this litigation process is relatively new, but it is expanding. Advertisements still circulate on a daily basis, and patient referrals for removal of mesh and tape continue to surface everywhere. Credentialing has become a major issue for concerned specialty societies [23], and courses to teach proper technique have intensified. Despite these efforts, it seems that the pendulum is shifting toward renewed scrutiny regarding the broad use of synthetic material in the vaginal wall. Even researchers with established credentials and track records are becoming concerned in light of the recent FDA release dated March 27,

2013, on sling tape for SUI [24] and emerging new scientific data [25].

1. Lessons learned

To be legally marketed, the main prerequisite across the world for a synthetic material is to demonstrate equivalence to existing devices that have been shown to be biocompatible and to go through, for example, the FDA’s premarket notification 510(k) process; such processes vary in different parts of the world. However, not all synthetic devices for POP or SUI are equal, and they should not reach the market without being used in carefully controlled clinical studies with adequate safety, efficacy, or adverse outcome data. Postmarket study surveillance (522 orders) on safety and effectiveness has now been mandated in the United States. In Europe this is currently the subject of contemporary discussion, but no similar formal process has been introduced.

Prior to surgery, a patient and her surgeon should have an adequate discussion that includes alternatives, benefits, risks, and complications [12,26,27] (Fig. 1). Surgery for SUI is effective and results in high rates of patient satisfaction [28,29]. Each patient should be offered nonsurgical alternatives, including pelvic floor muscle training. Although these nonsurgical treatments have lower efficacy, an individual patient should participate in her decision based on her own goals and preferences [30]. In addition, when a patient has made the decision to proceed with surgery, alternative surgical options that include non-mesh-based techniques should be offered, such as an autologous fascial sling or bladder neck suspension [31].

Surgeons should perform surgery for SUI or POP only if they are adequately trained in this subspecialist area, perform such surgery on a regular basis, and are aware of all potential therapeutic options. In particular, because complications differ based on the sling technique used, the advantages and the disadvantages should be outlined for each patient prior to final selection of a surgical technique. It is prudent to consider specifically adding the word *mesh* to a surgical consent for mesh-based procedures. In addition, in formulating their procedural recommendations, surgeons may wish to avoid certain risk profiles and consider the feasibility of repeated surgical treatment should the initial sling be unsuccessful. This is important for mesh slings that are placed for treatment and is an even more important discussion when a mesh-based sling is recommended for SUI prophylaxis [32], for which there is less information to inform the discussion of risks and benefits. In the only study to date, approximately six patients would require concomitant treatment during surgery for POP with TVT to prevent one patient from having SUI. Consequently, in our opinion, mesh materials should not be used prophylactically [33].

The evidence in the area of mesh-based slings in surgical practice is evolving rapidly. Surgeons should rely on reputable sources for unbiased information and evidence. In the absence of evidence, mesh-based procedures should be restricted to experimental or research settings until an

RECOMMENDATIONS FOR PATIENTS:**BEFORE SURGERY:**

Ask your surgeon about all SUI treatment options, including non-surgical options and surgical options that do and do not use mesh slings. It is important for you to understand why your surgeon may be recommending a particular treatment option to treat your SUI.

Any surgery for SUI may put you at risk for complications, including additional surgery. One complication that may occur when mesh slings are used is vaginal mesh erosion, which could require additional surgery to resolve.

If mesh erosion occurs through the vaginal tissue, it is possible that men may experience penile irritation and/or pain during sexual intercourse.

Ask your surgeon the following questions before you decide to have SUI surgery:

• What surgical or non-surgical treatment options are available and what do you recommend to treat my SUI?
• Have you had specialized training in the surgical treatment of SUI, and if so, what type of training have you had with this particular product and/or procedure?
• What can I expect after surgery and what is the recovery time?
• If I also have pelvic organ prolapse, will that change how you treat my SUI?
• What if the surgery doesn't correct my problem?
• Which side effects should I report to you after the surgery?
• Are you planning to use a mesh sling in my surgery? If so:
o How often have you performed this surgery using this particular product? What results have your other patients had with this product?
o What are the pros and cons of using a mesh sling in my particular case? How likely is it that my repair could be successfully performed without using a mesh sling?
o Are recovery times different for mesh sling surgery compared to non-mesh surgery?
o Will my partner be able to feel the mesh sling during sexual intercourse?
o If I have a complication related to the mesh sling, how likely is it that the complication can be resolved? Will you treat it or will I be referred to a specialist experienced with mesh sling complications?
o Is there patient information that comes with the product, and can I have a copy?

AFTER SURGERY:

Continue with annual check-ups and follow-up care, notifying your health care provider if complications develop, such as persistent vaginal bleeding or discharge, pelvic or groin pain, or pain during sexual intercourse. There is no need to take additional action if you are satisfied with your surgery and are not having complications or symptoms.

If you have complications or other symptoms:
Discuss complications and treatment options with your health care provider. Only your health care provider can give you personalized medical advice.
Consider getting a second opinion from a surgeon who specializes in female pelvic reconstruction if you are not satisfied with your discussion with your health care provider.

Let your health care provider know you have a mesh sling, especially if you plan to have another surgery, plan to become pregnant or have other medical procedures.

If you have had SUI surgery but do not know whether your surgeon used a mesh sling, ask your health care provider.

Talk to your health care provider about any additional questions you may have.

Fig. 1 – Information for patients with stress urinary incontinence. Reproduced with permission of the US Food and Drug Administration [27].

adequate body of information is available to support use in routine practice. Given the rapid adoption of mesh-based SUI procedures with limited long-term follow-up, continued reporting of longitudinal cohorts will be important. Registries should be organized on a national basis in collaboration with professional societies of all relevant disciplines. Such registries may be funded with innovative models of funding that involve industry support on a “per device” model and without any involvement in data collection or evaluation because such registries can be administered independently.

We are lacking an evidence-based approach to managing the wide variety of mesh-based complications. The use of such inclusive registries will allow the evaluation of complication outcomes. Although the clinical experience of subspecialty experts grows daily, stringently designed studies of important questions—for example, incise or excise obstructive mesh slings or use estrogen or excision for minor vaginal tape exposures and the management of erosion into the urinary tract, including the reconstruction of urethral–vaginal fistulae—remain unanswered. Classification of complications to allow comparison of reports [34] will assist research in this area. Significant subspecialty expertise improves the outcomes of such complex cases, and consideration should be given to working with national societies to establish a registry of accredited centers for the functional reconstruction of such complex cases.

2. The way forward

What is the future for use of synthetic material for mesh slings? It behooves all of us to spend a significant amount of time with our patients when considering a tape or mesh placement, along with clear documentation of all risks and known long-term complications and their management [35] (Appendix). In this context, it is essential to outline the other potential therapeutic options that are available. The scientific community has begun to acknowledge how matters can be improved [36] and is looking for solutions to better safeguard the public, including development of a certification process for specialists and “fellow” trainees. In addition, it is likely that the regulatory authorities will adopt more stringent regulations regarding evaluation of new devices before they are introduced into routine clinical practice.

Beyond the current, passionate debates for or against synthetic material, there is limited knowledge about the long-term integration of these devices into the vaginal wall near vital adjacent organs and the risks and benefits of the devices' added strength versus native tissue repair. So, is it the beginning of the end for mesh? This is unlikely because good results can be obtained by experienced hands, as long as patients are adequately informed about the pros and cons of using mesh devices, in particular, complications and lack of adequate long-term data. Certainly it is the beginning of more accountability on the part of physicians, the scientific community, and manufacturers to retain patients' trust and remove residual uncertainties. Future research should be directed at long-term alternatives using tissue-regeneration techniques and absorbable synthetic materials [37].

Conflicts of interest: Christopher R. Chapple is a speaker for Ranbaxy; a consultant for AMS, Lilly, and ONO; and a consultant, researcher, speaker, and trial participant for Allergan, Pfizer, and Recordati. The other authors have nothing to disclose.

Appendix – Take-home messages

- New surgical devices should be adequately assessed before introduction into clinical practice.

- Surgeons should carry out surgery for SUI only if they are adequately trained in the subspecialty and after appropriate evaluation of the patient.
- Although mesh insertion seems like an easy procedure, treating complications of mesh surgery may require extensive and complex procedures.
- Surgeons are not properly informing patients regarding their personal experience, number of cases done, and potential complications.
- Patients are not well informed. Patients should have more access to information about the potential complications of mesh.
- Complications are underreported. The reporting system for patients, physicians, and manufacturers should be improved.
- *Even with complete mesh removal, >30% of patients may be permanently disabled or may experience long-term symptoms.*

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